REMARKS

Entry of this Amendment is respectfully requested. Upon entry of this Amendment, claims 2-17, 19, 26, and 28 will be cancelled without prejudice or disclaimer of the subject matter recited therein and with the preserving of Applicant's right to submit the cancelled claims in one or more continuation and/or divisional applications; claims 1, 18, 20, 22, 25, and 27 will be amended; and claims 29-30 will be added. Claims 1, 18, 20-25, 27, 29, and 30 are pending.

Support for the instant amendments can be found throughout the specification and original claims, including, for example, original claim 19. In addition, support for the amendment can also be found, e.g., at paragraph [0011] on page 3, paragraphs [0016]-[0017] on page 4, paragraph [0073] on page 22, paragraph [0074] on pages 22-23, and paragraph [0080] on page 24. In addition, support for the amendment can be found, e.g., in U.S. Provision App. 60/462,120 to which the instant application claims priority, and which has been incorporated by reference in its entirety. For example, support for recitation of increased solubility of the active ingredient, i.e., ibuprofen, may be found at the paragraph bridging pages 1-2 of the provisional application. Support for new claims 29 and 30 may be found, e.g., at paragraphs [0014] and [0059] on pages 3 and 19, respectively.

Reconsideration and allowance of the application are respectfully requested.

Statement of Interview

Applicant expresses appreciation for the courtesies extended by Examiner Isis Ghali during a June 22, 2010 telephone interview with Applicant's representative Walter Schlapkohl. Applicant further notes that the Examiner Interview Summary mailed June 29, 2010 indicated that Mr. Stephen Roylance participated in the interview. However, solely to clarify the written record, Applicant notes that it was Mr. Schlapkohl, and not Mr. Roylance, who participated in the interview.

During the interview, Applicant's representative sought clarification with respect to various assertions set forth in the Office Action dated June 10, 2010. For example, Applicant's representative requested clarification with respect to the assertion on page 12, lines 7-9, that "it would have been obvious to use the clarified form of sesame oil *taught by Buyuktimkin* motivated by the desire to use a product that has advantageous properties of component of sesame oil" (emphasis added) because that art, i.e., *Buyuktimkin*, fails discloses clarified sesame

oil as an enhancer. The Examiner responded by indicating the Sharma teaches sesame oil.

During the interview, the patentability of the claims under consideration was also discussed, and the Examiner indicated that if Applicant were to include language relating to the increased solubility of ibuprofen with respect to clarified sesame oil and isopropyl myristate, and if Applicant were to incorporate the features, such as the ingredients and amounts, of claims 19 and 26 into claim 18, the Examiner would consider such an amendment in view of the entire record, including the evidence previously presented in the Declaration of Laura Spaulding pursuant to 37 C.F.R. §1.132.

During the interview, the Examiner further agreed to consider the color photographs which accompanied the Declaration of Laura Spaulding in a personal interview if necessary. The Examiner is accordingly invited to contact the undersigned in the event that a personal interview would advance prosecution.

Restriction Requirement

The Office Action states that the application contains claims 1-7, 13-17, and 20, which are drawn to an invention nonelected with traverse in the reply filed on December 19, 2007. The Office Action further indicates that a complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action.

In response, Applicant submits that with this Amendment, claims 2-7, 13-17, 19, 26, and 28 have been cancelled. Applicant further submits that although claim 20 was previously indicated as withdrawn in view of a species election requirement, claim 20 was included in Applicant's election of Group III, allegedly drawn to a method for treating pain comprising administering a transdermal composition as set forth in the Requirement for Restriction of November 19, 2007, at page 2, Section 1. Accordingly, Applicant submits that the instant Amendment is responsive and respectfully requests rejoinder of claim 20 with the elected subject matter upon indication that claim 18, from which claim 20 depends, is free of the art.

Applicant further notes that claim 1 has been amended to include all the ingredients and amounts as recited in (now cancelled) claims 19 and 26. Applicant further recognizes and appreciates that rejoinder of claim 1, which claim was not included amongst those claims in the elected Group III invention, is at the Examiner's discretion. Nevertheless, Applicant respectfully requests that the Examiner rejoin claim 1 with the elected subject matter, at least in view of the

foregoing amendments, which amendments are in conformance with language suggested by the Examiner in the interview of June 22, 2010.

Response To Claim Rejections – 35 U.S.C. § 103(a)

The Final Office Action rejects claims 18, 19, 21-25, 27, and 28 under 35 U.S.C. § 103(a) as allegedly unpatentable over the combination of Ramirez et al. (U.S. Patent No. 5,342,535; hereinafter "Ramirez"), Youssefyeh (U.S. Patent App. Pub. 2001/0036489 A1; hereinafter "Youssefyeh"), and Sharma et al. (U.S. Patent No. 5,229,130; hereinafter "Sharma").

The Final Office Action also rejects claim 26 under 35 U.S.C. § 103(a) as allegedly unpatentable over the combination of Ramirez, Youssefyeh, and Sharma, as applied to claims 18, 19, 21-25, 27, and 28, and further in view of Buyuktimkin et al. (U.S. Patent No. 6,083,996; hereinafter "Buyuktimkin").

Furthermore, although Applicant previously argued that the combination of sesame oil and ibuprofen in the presently claimed formulation quite unexpectedly provides an oil phase containing supersaturated ibuprofen, and that the supersaturation provides unexpectedly enhanced transdermal delivery potential, the Office asserts that the super-saturation of ibuprofen in sesame oil is not claimed. The rejection further alleges that the sesame oil taught by Buyuktimkin will display the same function as instantly claimed since materials and their properties are inseparable (Office Action at page 12, lines 18-20). Finally, in response to the Declaration of Laura Spaulding, the rejection asserts that "there is no showing that the objective evidence of nonobviousness is commensurate in scope with the claims," noting that (1) claims 18 and 25 recite clarified sesame oil, while the examples and the present declaration are directed to combination of sesame oil with isopropyl myristate, and (2) the unexpected results show an oil phase containing supersaturated ibuprofen, whereas the claims are directed to a tablet formulation (Office Action at page 13, lines 12-19).

In response, Applicant submits that the claimed subject matter is not unpatentable over Ramirez, Youssefyeh, Sharma, and/or Buyuktimkin, either alone or in combination. However, solely to advance prosecution of the application and without acquiescing to the propriety of the rejections, Applicant submits that claims have been amended as suggested by the Examiner during the above-discussed interview of June 22, 2010. Applicant further submits that none of

the cited documents, either alone or in combination, teaches or suggests "[a] method of treating and/or alleviating at least one of pain, aches, and inflammation comprising,

dissolving in a bath a pharmaceutical composition for transdermal delivery in the form of a tablet, said tablet being prepared from a composition comprising a mixture of ibuprofen, clarified sesame oil, and isopropyl myristate wherein the solubility of ibuprofen is increased,

wherein the pharmaceutical composition comprises:

at least one skin permeation enhancer comprising clarified sesame oil and isopropyl myristate in an amount from about 1% to about 5% by weight based on the total weight of the composition;

at least one effervescent agent in an amount from about 30% to about 70% by weight based on the total weight of the composition;

at least one active ingredient or pharmaceutically acceptable salt thereof comprising ibuprofen in an amount from about 1% by weight to about 10% by weight based on the total weight of the composition; and

at least one acid agent present in an amount from about 20% to about 40% by weight based on the total weight of the composition; and

immersing a body part of a human being to be treated in the bath containing the dissolved pharmaceutical composition." In particular, Applicant submits that the cited art, either alone or in combination, fails to suggest at least the particular combination of ibuprofen and clarified sesame oil in a composition for transdermal delivery, much less such a composition in which the solubility of ibuprofen is increased.

Furthermore, Applicant submits that the presently claimed subject matter is directed to, *inter alia*, a composition comprising clarified sesame seed oil, ibuprofen, and isopropyl myristate. Thus, Applicant submits that the claimed subject matter is commensurate in scope with objective evidence previously submitted, including the unexpected results which show that the presently claimed formulation provides increased solubility of ibuprofen in a mixture of sesame oil and isopropyl myristate. Applicant further submits that the increased solubility of the ibuprofen provides unexpectedly enhanced transdermal delivery potential.

Applicant also submits that it is of no moment that the evidence shows increased solubility of ibuprofen in an oil phase, whereas the claimed subject matter is directed to a tablet, at least in view of the disclosure in the specification, which discloses *inter alia*, that two skin

permeation enhancers may be blended, and then heated to a temperature of about 40°C (see, e.g., specification at page 22, paragraph [0074]; Applicant notes that the mixtures as shown in the Declaration of Laura Spaulding were also heated to 40°C). The specification further discloses that the active ingredient may then be added to the enhancer mixture and mixed until the desired dissolution of the active ingredient is achieved (specification at page 22, paragraph [0074]). The enhancer mixture may then be combined with an effervescent mixture such that the final mixture possesses a flaky consistency which may be pressed into tablet molds. *Id.* Accordingly, the unexpected results presented by Applicant are applicable to any composition for transdermal delivery as claimed.

Furthermore, with regard to claim 30, Applicant submits that Ramirez discloses an analgesic soak tablet comprising mineral oil and menthol in a ratio of 2.0:1.0. However, Ramirez fails to disclose a tablet wherein the at least one skin permeation enhancer and the at least one active ingredient are present in a weight ratio from about 1.0:2.0 to about 0.5:3.0.

Based at least on the foregoing, including the unexpectedly high saturation of ibuprofen in sesame oil and isopropyl myristate, Applicant submits that the claimed subject matter is not unpatentable over Ramirez, Youssefyeh, Sharma, and/or Buyuktimkin, either alone or in combination. Applicant respectfully requests reconsideration of the rejections under 35 U.S.C. § 103(a), and withdrawal of the same.

Response to Advisory Action

The Advisory Action dated August 10, 2010, indicates that "the amended claims remain rejected under the combination of Ramirez et al. (US 5,342,535), Youssefyeh (US 2001/0036489), Sharma et al. (US 5,229,130), and Buyuktimkin (US 6,083,996)." The Advisory Action further alleges that recitation of a "tablet being prepared from a composition comprising a solution of ibuprofen, clarified sesame oil, and isopropyl myristate such that the solubility of ibuprofen is increased" introduces new matter, and that such a limitation has not been found in the specification or in the provisional application referred to for support.

In response, Applicant submits the following remarks to supplement the remarks regarding those portions of the specification and those portions of the provisional application which support recitation of a "tablet being prepared from a composition comprising a mixture of ibuprofen, clarified sesame oil, and isopropyl myristate wherein the solubility of ibuprofen is

increased." Applicant is also submitting the following remarks in response to the Advisory Action's assertion that the amended claims remain rejected over the combination of Ramirez, Youssefyeh, Sharma and Buyuktimkin.

New Matter

With regard to the alleged new matter, Applicant notes that support for "a composition comprising a mixture of ibuprofen, clarified sesame oil, and isopropyl myristate" can be found throughout the specification and original claims, including, for example, at paragraph [0011] on page 3 of the specification, which discloses that "[t]he present invention provides a pharmaceutical **composition** for transdermal delivery comprising at least one skin permeation enhancer and at least one active ingredient or pharmaceutically acceptable salt thereof" (emphasis added). Paragraph [0016] on page 4 discloses that the skin permeation enhancer may comprise, *inter alia*, **isopropyl myristate**, **clarified sesame oil**, and mixtures thereof (emphasis added). Paragraph [0017] on page 4 discloses that the active ingredient may comprise **ibuprofen** (emphasis added).

Paragraph [0073] on page 22 of the specification discloses that "[t]he composition of the present invention is prepared in a process that includes combining at least one skin permeation enhancer in an enhancer mixture with at least one active ingredient or pharmaceutically acceptable salt thereof. To aid in **dissolution** of the active ingredient, the enhancer mixture is heated to any temperature to accommodate dissolution of the active ingredient so long as the temperature does not cause decomposition of the active ingredient. The dissolution of the active ingredient in the present invention may be controlled by modification of the skin permeation enhancer" (emphasis added).

Paragraph [0074] bridging pages 22-23 provides even more detailed description of how such a composition may be manufactured:

> More preferably, the composition of the present invention is prepared by blending two effervescent agents until well mixed to make up the effervescent mixture. The effervescence allows effective dispersion of the composition of the present invention in water. **Two skin permeation enhancers are then blended until homogeneous to make up the enhancer mixture. The enhancer mixture is heated to a temperature of about 40°C. An active ingredient is then added to the enhancer mixture and mixed until desired dissolution of the active ingredient is achieved.** The enhancer mixture is

> combined with the effervescent mixture until well blended, and the final mixture possesses a flaky consistency. The final flaky mixture is pressed into **tablet** molds. The tablets are pressed using a tablet press according to methods known in the art, and allowed to dry for a few hours. The result is an effervescent tablet which when dissolved in water (such as bathtub water), allows the skin permeation enhancers to adsorb to the skin and allow transdermal delivery of the active ingredient (emphasis added).

Increasing the solubility of the active ingredient is therefore disclosed in various forms and portions of the specification, including as set forth above, as well as, for example, at paragraph [0080] on page 24, which discloses that **"isopropyl myristate and clarified sesame oil may be modified to increase the dissolution of the active ingredient in the composition"** (emphasis added). Furthermore, additional support for the amendment can also be found in U.S. Provision App. 60/462,120 to which the instant application claims priority, and which has been incorporated by reference in its entirety. For example, support for recitation of increased solubility of the active ingredient, i.e., ibuprofen, may be found at the paragraph bridging pages 1-2 of the provisional application. In particular, Applicant notes that the above-cited portion of the provisional application discloses mixtures comprising ibuprofen, isopropyl myristate, and clarified sesame oil, and that the concentration of the isopropyl myristate and clarified sesame oil may be modified **"so that solubility of the dissolved active ingredient is altered"** (emphasis added).

Applicant also submits that Example 1 of the specification of the instant non-provisional application specifically discloses a tablet comprising ibuprofen, isopropyl mystate and clarified sesame oil.

Based at least on the foregoing, Applicant submits that the claimed subject matter, including recitation of a "tablet being prepared from a composition comprising a mixture of ibuprofen, clarified sesame oil, and isopropyl myristate wherein the solubility of ibuprofen is increased" does not introduce new matter.

Obviousness

With regard to the Advisory Action's assertion that "the amended claims remain rejected under the combination of Ramirez et al. (US 5,342,535), Youssefyeh et al. (US 2001/0036489), Sharma et al. (US 5,229,130), and Buyutimkim (US 6,083,996)," Applicant submits that none of the cited documents, either alone or in combination, teaches or suggests the methods or products

as claimed. In particular, Applicant submits that the cited art, either alone or in combination, fails to suggest at least the particular combination of ibuprofen, clarified sesame oil, and isopropyl myristate in a composition for transdermal delivery, much less such a composition in which the solubility of ibuprofen is increased.

Based at least on the foregoing, Applicant submits that the claimed subject matter is not obvious over Ramirez, Youssefyeh, Sharma, and/or Buyuktimkin, either alone or in combination.

CONCLUSION

In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow all the pending claims.

No fee is believed due at this time. If, however, any additional fee is necessary to ensure consideration of the submitted materials, the Patent and Trademark Office is hereby authorized to charge the same to Deposit Account No. 19-0089.

Any comments or questions concerning this application can be directed to the undersigned at the telephone number given below.

Respectfully Submitted,
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